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Derivation of Candidates for the Combat Casualty Critical Care (C4) Database

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ABSTRACT Objective: To describe the development of the Combat Casualty Critical Care Database, a comprehensive database of critically injured combat casualties to identify potentially modifiable risk factors for morbidity and mortality in this population. Methods: The Department of Defense's Joint Theater Trauma Registry was queried for all combat casualties injured from February 1, 2002 through February 1, 2011. The search was limited to patients who required admission to the intensive care unit and survived to be evacuated to Landstuhl Regional Medical Center. Results: The query yielded 6,011 patients. The mean age was 25.7± 6.2 years. The majority of patients were male (98.3%), injured in Iraq (80%) and were members of the U. S. Army (72.6%). Most patients (58.0%) had an injury severity score in the lowest severity category (0–15). The mortality rate was 1.8%. The median day of death after injury (interquartile range) was 6 (3–14). Conclusions: We identified a cohort of critically wounded combat casualties that encompasses the majority of such patients injured in the course of the wars in Iraq and Afghanistan. When this database is fully populated, rigorous epidemiologic analysis will seek to identify factors associated with morbidity and mortality to improve future care.

INTRODUCTION

Great strides have been made in the care of wounded warriors during the modern conflicts in Iraq and Afghanistan. Prehospital tourniquet use,[1,2] damage control resuscitation/surgical practices,[3–5] and rapid global evacuation[6] have all contributed to survival rates unprecedented in the history of warfare. Research in the military setting has primarily targeted the first two peaks of the classic three-peak model[7] of trauma mortality; the immediate and early deaths resulting predominantly from hemorrhage. Although some evidence suggests that the latter third peak of mortality after trauma is decreasing,[8] this has not been evaluated in wounded warriors. Notably, one study that retrospectively analyzed 558 fatality records of casualties that died of wounds after admission to a military treatment facility judged that 51.4% sustained potentially survivable injuries if treated under ideal circumstances.[9]

The Joint Theater Trauma Registry (JTTR) is the source reference for the majority of epidemiologic work done to date in the combat casualty care population.[10–12] Although the JTTR is an excellent resource for basic epidemiologic studies, the clinical data that can be abstracted for each individual casualty is limited. For example, all diagnoses in JTTR are based on documentation by treating physicians. This is analogous to using International Classification of Diseases-9 codes that have been shown to be inaccurate for the purposes of epidemiologic studies.[13] Furthermore, laboratory data from the JTTR are limited to blood gases, international normalized ratios, hemoglobin, hematocrit, and platelets at admission to and discharge from the military treatment facility. This hinders the ability to use the registry data to discriminate specific factors identifiable in the intensive care unit (ICU) that may portend increased morbidity and mortality in this unique population.

The purpose of this article is to inform the military research community of the authors' plans to construct the Combat Casualty Critical Care (C4) Database, a detailed clinical database that can be used for more complex epidemiologic studies of critically injured war fighters. The basic demographic and injury characteristics of the cohort are also reported. The data collected from this study cannot be made freely available given the limits of our regulatory approval. However, we invite other researchers to contact us for potential collaborations involving this new database.

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METHODS

Study approval was granted by the U.S. Army Medical Research and Materiel Command Institutional Review Board. The study was assessed as minimal risk and a waiver of informed consent was granted. Phase I of the study involved identification of patients from the JTTR. Inclusion criteria for the JTTR query were all U.S. active duty military patients with battle injuries sustained in Iraq or Afghanistan that were admitted to an ICU as some point in their initial

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TABLE I. List and description of sources for the Combat Casualty Critical Care (C4) Database

Data Source	Description
Composite Health Care System	Serves as the foundation for the Military Electronic Medical Record. Allows electronic ordering and review of laboratories and medications
Essentris	Primary inpatient medical record system at Military Treatment Facilities
Armed Forces Health Longitudinal Technology Application	Worldwide electronic medical record system used for the documentation and review of outpatient encounters
COLLECTOR	Comprehensive database of trauma and burn patients admitted to the San Antonio Military Medical Center and the U. S. Army Institute of Surgical Research Burn Unit
Department of Defense medical mortality registry	Comprehensive registry of active duty deaths compiled by the Office of the Armed Forces Medical Examiner, Armed Forces Institute of Pathology
Medical Communications for Combat Casualty Care	In-theater version of Composite Health Care System
Theater Medical Data Store	Online database that include history, progress notes, laboratories, drug and radiologic studies done in theater

hospitalization. Nonactive duty personnel, active duty personnel evacuated from a location other than Iraq or Afghanistan, and those with nonbattle injury were excluded. Because we wanted to look at late death after trauma, patients who did not survive to be evacuated to Landstuhl Regional Medical Center were also excluded. The period queried was February 1, 2002 through February 1, 2011.

As previously discussed, patient-specific clinical data that can be gleaned from the JTTR is limited. Therefore, in Phase II of the study, multiple additional clinical data sources (Table I) accessible from theater, San Antonio Military Medical Center, Walter Reed National Military Medical Center, and Landstuhl Regional Medical Center will be queried and the abstracted data consolidated into a single database. The variables that will be collected are listed in Table II. Patient identifiers (name and social security number) will be required to merge the data from these multiple sources. One author (JAJ) will be responsible for assembling and maintaining the database. Given that the data will be coming from multiple different sources, several authors will be involved in vetting the data to ensure that it is consistent in its final form (IJS, BDM, and KKC).

Following data collection, analysis will occur in the following fashion. Overall standard descriptive statistical methods will be used to analyze data; any categorical variables from each group will be compared via χ^2 analysis while continuous variables will be compared via Student's t test or Wilcoxon test as appropriate. Multiple logistic regression will be performed to analyze the relationship between independent and dependent variables, to adjust for potential confounding and to evaluate interaction effects. Independent variables will consist of those factors hypothesized to be associated with the outcomes of interest. The dependent variables will be mortality, days on mechanical ventilation, days in the ICU, and days in the hospital. Factors found not to be statistically significant ($p > 0.1$) will be removed from the model via backward elimination. A similar method will also be used to determine independent risk factors for acute kidney injury (AKI) and acute respiratory distress syndrome (ARDS).

TABLE II. Data to Be Collected From Participating Institutions

Demographic factors: age, race, sex
Admission date (to each participating center)
Date of injury
Laboratories: serum creatinine, complete blood counts, cultures (wound, blood, urine, sputum, CSF, or other bodily fluid culture), creatinine kinase, myoglobin (serum and urine), lactate, prealbumin, C-reactive protein, and erythrocyte sedimentation rate
Injury Severity Score
GCS at presentation
Mechanism of injury
Presence of traumatic brain injury (by Barrel level)
Amputation (with level)
Blood products (packed red blood cells, platelets, fresh frozen plasma, whole blood)
Presence of acute respiratory distress syndrome
Use of renal replacement therapy
Oliguria (<450 cc/24 hour)
Anuria (<100 cc/24 hour)
Use of vasoactive meds
Contrasted radiologic studies
Insulin requirement
Comorbid diagnoses: diabetes, coronary artery disease, chronic kidney disease, peripheral vascular occlusive disease
Use of antihypertensive medications
TBSA burned
Full thickness TBSA
Fluid resuscitation (volume and type administered)
Acute kidney injury (by AKIN and RIFLE)
Use of renal replacement therapies
Use of nephrotoxic agents
Ventilator days
ICU days
Hospital days
Mortality

CSF, Cerebrospinal fluid; GCS, Glasgow coma scale; AKIN, Acute Kidney Injury Network; RIFLE, Risk, Injury, Failure, Loss, End-stage renal disease; TBSA, Total body surface area.

RESULTS

The query yielded 6,011 patients for study inclusion. The characteristics of this population are summarized in Table III.

TABLE III. Baseline Characteristics of Patient Cohort

Age (Mean ± SD)	25.7 ± 6.2
Male (Number [Percentage])	5908 (98.3%)
Military Operation (Number [Percentage])	
OEF	1202 (20.0%)
OIF	4798 (79.8%)
OND	11 (0.2%)
ISS (Number [Percentage])	
0–15	3486 (58.0%)
16–25	1373 (22.8%)
26–55	1078 (17.9%)
>55	74 (1.2%)
Burn Injury (Number [Percentage])	1000 (16.6%)
Service (Number [Percentage])	
Army	4363 (72.6%)
Marines	1429 (23.8%)
Navy	148 (2.5%)
Air Force	71 (1.2%)
Dominant Injury Type (Number [Percentage])	
Blunt	3235 (53.8%)
Burn	143 (2.4%)
Penetrating	2630 (43.8%)
Other/Unknown	3 (0.1%)
Dominant Mechanism of Injury (Number [Percentage])	
Explosive Device	4686 (78.0%)
Gunshot wound	1145 (19.0%)
Other	180 (3%)
Mortality (number [percentage])	110 (1.8%)
Days from injury to death (median [IQR])	6 (3–14)

SD, Standard deviation; OEF, Operation enduring freedom; OIF, Operation Iraqi Freedom; OND, Operation New Dawn; ISS, Injury severity score; IQR, interquartile range.

The majority were male (98.3%) with an average age of 25.7 ± 6.2 years. The majority of patients (78.0%) were injured by an explosive device and had an injury severity score (ISS) in the lowest severity category (58.0%). Most patients were injured during combat operations in Iraq (80%). Patients with any burn injury compromised 16.6% of the cohort. One hundred and ten patients (1.8%) died. The median day of death after injury (interquartile range) was 6 (3–14). These data will be merged with data from the sources listed above to complete the full database.

DISCUSSION

We identified the complete population of critically injured combat patients during 9 years of the course of the wars in Iraq and Afghanistan. In-depth analysis of detailed data from this cohort will contribute to enhanced understanding of the risk factors for morbidity and mortality, facilitate comparisons between combat-injured patients and the civilian trauma population, and serve as a baseline for long-term follow-up studies.

A variety of factors have been reported to be independently associated with late mortality after trauma. One such factor is AKI. The association of AKI with wounded warrior outcomes has only been examined by one modern study.[14] This study analyzed a cohort of 692 patients with burn injury sustained in support of combat operations in Iraq and Afghanistan. The AKI incidence was 29.9% and was strongly associated with mortality in a multivariate model. In the civilian trauma population, AKI occurs in 18–37% of patients in the post-traumatic setting and is also independently associated with mortality.[15–17] Factors associated with AKI in the civilian trauma population include age, female sex, African–American race, comorbidities, non-TBI-related trauma, body mass index, unmatched red blood cell transfusion, APACHE III score, and Abbreviated Injury Score.[15,17] One common risk factor for AKI in the general, nontrauma population is contrast-induced nephropathy.[18] Interestingly, contrast-induced nephropathy does not significantly contribute to AKI in the civilian trauma population.[19,20] Analysis of our cohort could confirm these findings in the wounded warrior population.

Development of ARDS is associated with increased mortality in trauma patients.[21] Several factors associated with ARDS development include red blood cell transfusion within the first 24 hours, ISS > 28, chest trauma, and femoral fracture.[21,22] Notably, trauma remote to the lungs can induce lung damage via systemically increased cytokines such as interleukin 6.[23] Other factors associated with increased mortality in the civilian population in addition to AKI and ARDS include the use of vasopressors, measures of injury severity, transfusion requirement, and multiorgan failure (MOF).[16,24,25] In intubated casualties receiving a blood transfusion, increasing plasma and crystalloid volume independently predict development of ARDS[26] which increases the risk of death nearly 5-fold in combat casualties.[27] Rigorous and detailed statistical analysis of this database, with its large sample size of subjects, will assist in determining which of these factors are independently associated with mortality in patients critically injured in combat.

This patient cohort can also serve as a basis for examining the long-term implications of combat injury. It is increasingly recognized that the occurrence of an acute illness can impact long-term health and quality of life. A single episode of traumatic injury is associated with long-term mortality when compared to the population at large, driven mostly by suicide and repeat trauma.[28] AKI has been associated with a higher likelihood of patient discharge to a rehabilitation facility, rather than home, after trauma.[15] In addition, an episode of AKI has been associated with chronic kidney disease, end-stage renal disease, and increased long-term mortality in a variety of nontrauma populations.[29–31] The increased risk of mortality after an episode of AKI persists years after the initial insult. For example, in a large cohort of Veterans Administration patients, mortality increased across AKI Network stages years after the original episode of AKI with the highest hazard ratios in the youngest age group.[30] There is also evidence that an episode of ARDS is associated with poor long-term outcomes. Despite normal pulmonary function tests, patients with a history of ARDS exhibit decreased function (as defined by 6-minute walk test and self-report of

function on a validated questionnaire).[32] Again, these findings were present years after the initial insult. Finally, MOF also results in poor long-term outcomes. One study (with a trauma patients as a substantial portion of the cohort) demonstrated that patients with previous MOF had increased mortality and needed more assistance with activities of daily living compared to those without MOF.[33] If AKI, ARDS, and/or MOF are common in this cohort of patients, it implies an important cause of long-term disease burden warranting future longitudinal study. The cohort identified by this study provides the foundation for this further work. Analysis of the long-term outcomes in this cohort will have a profound impact on both the Departments of Defense and Veterans Administration health systems related to resource requirements and allocation.

CONCLUSION

We identified a cohort of 6,011 patients with battle injury that required ICU level care. When fully populated, the C4 database will comprehensively describe the critically injured combat population and facilitate rigorous statistical analysis to elucidate factors associated with mortality and morbidity. The results will likely focus additional research on critically ill patients with combat injury to improve the care and outcomes of future wartime casualties. Furthermore, long-term follow-up of this patient cohort could assist in their continued care ensuring that their sacrifices in our Nation's last decade of war are not forgotten.

> "With malice toward none, with charity for all, with firmness in the right as God gives us to see the right, let us strive on to finish the work we are in, to bind up the nation's wounds, to care for him who shall have borne the battle and for his widow and his orphan, to do all which may achieve and cherish a just and lasting peace among ourselves and with all nations."
>
> Abraham Lincoln, Second Inaugural Address, March 4, 1865

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